WHAT IS CLAIMED IS:

1. An isolated DNA comprising a sequence of SEQ ID NO:1 as altered by one or more mutations selected from the group consisting of A332G, G478A, G521A, G535A, G580C, C727T, T742C, T797C, G921+1T, A922-2C, G928A, C1046G, C1066T, G1097A, C1172T, C1343G, C1588T, C1697T, C1747T and G1781A.

2. A nucleic acid probe specifically hybridizable to a human mutated *KVLQT1* and not to wild-type DNA, said mutated *KVLQT1* comprising a mutation of SEQ ID NO:1 selected from the group consisting of A332G, G478A, G521A, G535A, G580C, C727T, T742C, T797C, G921+1T, A922-2C, G928A, C1046G, C1066T, G1097A, C1172T, C1343G, C1588T, C1697T, C1747T and G1781A.

3. A method for detecting a mutation in *KVLQT1* said mutation selected from the group consisting of A332G, G478A, G521A, G535A, G580C, C727T, T742C, T797C, G921+1T, A922-2C, G928A, C1046G, C1066T, G1097A, C1172T, C1343G, C1588T, C1697T, C1747T and G1781A which comprises analyzing a sequence of said gene or RNA from a human sample or analyzing the sequence of cDNA made from mRNA from said sample.

4. The method of claim 3 wherein said mutation is detected by a method selected from the group consisting of:

a) hybridizing a probe specific for one of said mutations to RNA isolated from said human sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said mutation in the sample;

b) hybridizing a probe specific for one of said mutations to cDNA made from RNA isolated from said sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said mutation in the sample;

c) hybridizing a probe specific for one of said mutations to genomic DNA isolated from said sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said mutation in the sample;

d) amplifying all or part of said gene in said sample using a set of primers to produce amplified nucleic acids and sequencing the amplified nucleic acids;

e) amplifying part of said gene in said sample using a primer specific for one of said mutations and detecting the presence of an amplified product, wherein the presence of said product indicates the presence of said mutation in the sample;

f) molecularly cloning all or part of said gene in said sample to produce a cloned nucleic acid and sequencing the cloned nucleic acid;

g) amplifying said gene to produce amplified nucleic acids, hybridizing the amplified nucleic acids to a DNA probe specific for one of said mutations and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said mutation;

h) forming single-stranded DNA from a gene fragment of said gene from said human sample and single-stranded DNA from a corresponding fragment of a wild-type gene, electrophoresing said single-stranded DNAs on a non-denaturing polyacrylamide gel and comparing the mobility of said single-stranded DNAs on said gel to determine if said single-stranded DNA from said sample is shifted relative to wild-type and sequencing said single-stranded DNA having a shift in mobility;

i) forming a heteroduplex consisting of a first strand of nucleic acid selected from the group consisting of a genomic DNA fragment isolated from said sample, an RNA fragment isolated from said sample and a cDNA fragment made from mRNA from said sample and a second strand of a nucleic acid consisting of a corresponding human wild-type gene fragment, analyzing for the presence of a mismatch in said heteroduplex, and sequencing said first strand of nucleic acid having a mismatch;

j) forming single-stranded DNA from said gene of said human sample and from a corresponding fragment of an allele specific for one of said mutations, electrophoresing said single-stranded DNAs on a non-denaturing polyacrylamide gel and comparing the mobility of said single-stranded DNAs on said gel to determine if said single-stranded DNA from said sample is shifted relative to said allele, wherein no shift in electrophoretic mobility of the single-stranded DNA relative to the allele indicates the presence of said mutation in said sample; and

k) forming a heteroduplex consisting of a first strand of nucleic acid selected from the group consisting of a genomic DNA fragment of said gene isolated from said sample, an RNA fragment isolated from said sample and a cDNA fragment made from mRNA from said sample and a second strand of a nucleic acid consisting of a corresponding gene allele fragment specific for one of said mutations and analyzing for the presence of a mismatch in said heteroduplex, wherein no mismatch indicates the presence of said mutation.

5. A method according to claim 4 wherein hybridization is performed *in situ*.

6. An isolated human polypeptide encoded by *KVLQT1* comprising a mutation of SEQ ID NO:2 selected from the group consisting of Y111C, E160K, R174H, G179S, A194P, R243C, W248R, L266P, V307sp, V310I, S349W, Q356X, R366Q, T391I, P448R, Q530X, S566F, R583C and R594Q.

7. An antibody capable of binding the polypeptide of claim 6 but incapable of binding a wild-type polypeptide.

8. An antibody according to claim 7 wherein said antibody is a monoclonal antibody.

9. A method of assessing a risk in a human subject for long QT syndrome which comprises screening said subject for a mutation in *KVLQT1* by comparing the sequence of said *KVLQT1* or its expression products isolated from a tissue sample of said subject with a wild-type sequence of said *KVLQT1* or its expression products, wherein a mutation in the sequence of the subject indicates a risk for long QT syndrome.

10. The method of claim 9 wherein said expression product is selected from mRNA of said gene or a polypeptide encoded by said gene.

11. The method of claim 9 wherein one or more of the following procedures is carried out:

(a) observing shifts in electrophoretic mobility of single-stranded DNA from said sample on non-denaturing polyacrylamide gels;

(b) hybridizing a probe to genomic DNA isolated from said sample under conditions suitable for hybridization of said probe to said gene;

(c) determining hybridization of an allele-specific probe to genomic DNA from said sample;

(d) amplifying all or part of said gene from said sample to produce an amplified sequence and sequencing the amplified sequence;

(e) determining by nucleic acid amplification the presence of a specific mutant allele in said sample;

(f) molecularly cloning all or part of said gene from said sample to produce a cloned sequence and sequencing the cloned sequence;

(g) determining whether there is a mismatch between molecules (1) said gene genomic DNA or mRNA isolated from said sample, and (2) a nucleic acid probe complementary to the human wild-type gene DNA, when molecules (1) and (2) are hybridized to each other to form a duplex;

(h) amplification of said gene sequences in said sample and hybridization of the amplified sequences to nucleic acid probes which comprise wild-type gene sequences;

(i) amplification of said gene sequences in said tissue and hybridization of the amplified sequences to nucleic acid probes which comprise said mutant gene sequences;

(j) screening for a deletion mutation;

(k) screening for a point mutation;

(l) screening for an insertion mutation;

(m) determining *in situ* hybridization of said gene in said sample with one or more nucleic acid probes which comprise said gene sequence or a mutant sequence of said gene;

(n) immunoblotting;

(o) immunocytochemistry;

(p) assaying for binding interactions between said gene protein isolated from said tissue and a binding partner capable of specifically binding the polypeptide expression product of a mutant allele and/or a binding partner for the polypeptide; and
(q) assaying for the inhibition of biochemical activity of said binding partner.

12. A nucleic acid probe which hybridizes to the isolated DNA of claim 1 under conditions at which it will not hybridize to wild-type DNA.

13. A method for diagnosing a mutation which causes long QT syndrome comprising hybridizing a probe of claim 12 to a patient's sample of DNA or RNA, the presence of a hybridization signal being indicative of long QT syndrome.

14. A method according to claim 13 wherein the patient's DNA or RNA has been amplified and said amplified DNA or RNA is hybridized with a probe of claim 12.

15. A method according to claim 13 wherein said hybridization is performed *in situ*.

16. A method according to claim 13 wherein said assay is performed using nucleic acid microchip technology.

17. A method for diagnosing a mutation which causes long QT syndrome comprising amplifying a region of gene or RNA for *KVLQT1* and sequencing the amplified gene or RNA wherein long QT syndrome is indicated by any one or more mutations selected from the group consisting of A332G, G478A, G521A, G535A, G580C, C727T, T742C, T797C, G921+1T, A922-2C, G928A, C1046G, C1066T, G1097A, C1172T, C1343G, C1588T, C1697T, C1747T and G1781A.

18. A method for diagnosing a mutation which causes long QT syndrome comprising identifying a mismatch between a patient's DNA or RNA and a wild-type DNA or RNA probe wherein said probe hybridizes to a region of DNA or RNA wherein said region comprises a mutation of SEQ ID NO:1 selected from the group consisting of A332G,

G478A, G521A, G535A, G580C, C727T, T742C, T797C, G921+1T, A922-2C, G928A, C1046G, C1066T, G1097A, C1172T, C1343G, C1588T, C1697T, C1747T and G1781A.

19. The method of claim 18 wherein the mismatch is identified by an RNase assay.

20. A method for diagnosing long QT syndrome said method consisting of an assay for the presence of mutant KVLQT1 polypeptide in a patient by reacting a patient's sample with an antibody of claim 7, the presence of a positive reaction being indicative of long QT syndrome.

21. The method of claim 20 wherein said assay comprises immunoblotting.

22. The method of claim 20 wherein said assay comprises an immunocytochemical technique.

23. A method for diagnosing long QT syndrome, said method comprising analyzing a KVLQT1 polypeptide, a mutation in said polypeptide being indicative of long QT syndrome wherein said mutation is a mutation selected from the group consisting of Y111C, E160K, R174H, G179S, A194P, R243C, W248R, L266P, V307sp, V310I, S349W, Q356X, R366Q, T391I, P448R, Q530X, S566F, R583C and R594Q.

24. A method to screen for drugs which are useful in treating a person with a mutation in *KVLQT1* wherein said mutation is selected from the group consisting of A332G, G478A, G521A, G535A, G580C, C727T, T742C, T797C, G921+1T, A922-2C, G928A, C1046G, C1066T, G1097A, C1172T, C1343G, C1588T, C1697T, C1747T and G1781A, said method comprising:

a) placing a first set of cells expressing KVLQT1 with a mutation, wherein said mutation is selected from the group consisting of Y111C, E160K, R174H, G179S, A194P, R243C, W248R, L266P, V307sp, V310I, S349W, Q356X, R366Q, T391I, P448R, Q530X, S566F, R583C and R594Q, into a bathing solution;

b) inducing a first induced K^+ current in the cells of step (a);

c) measuring said first induced K^+ current;

d) placing a second set of cells expressing wild-type KVLQT1 into a bathing solution

e) inducing a second induced K^+ current in the cells of step (d);

f) measuring said second induced K^+ current;

g) adding a drug to the bathing solution of step (a);

h) inducing a third induced K^+ current in the cells of step (g);

i) measuring said third induced K^+ current; and

j) determining whether the third induced K^+ current is more similar to the second induced K^+ current than is the first induced K^+ current, wherein drugs resulting in a third induced K^+ current which is closer to the second induced K^+ current than is the first induced K^+ current are useful in treating said persons.

25. An isolated DNA encoding a KVLQT1 polypeptide of SEQ ID NO:2 having a mutation selected from the group consisting of Y111C, E160K, R174H, G179S, A194P, R243C, W248R, L266P, V307sp, V310I, S349W, Q356X, R366Q, T391I, P448R, Q530X, S566F, R583C and R594Q.

26. An isolated DNA comprising a sequence of SEQ ID NO:3 as altered by one or more mutations selected from the group consisting of G3340A, C4501G, del4850-4852, G4868T, G5349A and G5360A.

27. A nucleic acid probe specifically hybridizable to a human mutated *SCN5A* and not to wild-type DNA, said mutated *SCN5A* comprising a mutation of SEQ ID NO:3 selected from the group consisting of G3340A, C4501G, del4850-4852, G4868T, G5349A and G5360A.

28. A method for detecting a mutation in *SCN5A* said mutation selected from the group consisting of G3340A, C4501G, del4850-4852, G4868T, G5349A and G5360A which comprises analyzing a sequence of said gene or RNA from a human sample or analyzing the sequence of cDNA made from mRNA from said sample.

29. The method of claim 28 wherein said mutation is detected by a method selected from the group consisting of:

a) hybridizing a probe specific for one of said mutations to RNA isolated from said human sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said mutation in the sample;

b) hybridizing a probe specific for one of said mutations to cDNA made from RNA isolated from said sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said mutation in the sample;

c) hybridizing a probe specific for one of said mutations to genomic DNA isolated from said sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said mutation in the sample;

d) amplifying all or part of said gene in said sample using a set of primers to produce amplified nucleic acids and sequencing the amplified nucleic acids;

e) amplifying part of said gene in said sample using a primer specific for one of said mutations and detecting the presence of an amplified product, wherein the presence of said product indicates the presence of said mutation in the sample;

f) molecularly cloning all or part of said gene in said sample to produce a cloned nucleic acid and sequencing the cloned nucleic acid;

g) amplifying said gene to produce amplified nucleic acids, hybridizing the amplified nucleic acids to a DNA probe specific for one of said mutations and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said mutation;

h) forming single-stranded DNA from a gene fragment of said gene from said human sample and single-stranded DNA from a corresponding fragment of a wild-type gene, electrophoresing said single-stranded DNAs on a non-denaturing polyacrylamide gel and comparing the mobility of said single-stranded DNAs on said gel to determine if said single-stranded DNA from said sample is shifted relative to wild-type and sequencing said single-stranded DNA having a shift in mobility;

i) forming a heteroduplex consisting of a first strand of nucleic acid selected from the group consisting of a genomic DNA fragment isolated from said sample, an RNA fragment isolated from said sample and a cDNA fragment made from mRNA from said

sample and a second strand of a nucleic acid consisting of a corresponding human wild-type gene fragment, analyzing for the presence of a mismatch in said heteroduplex, and sequencing said first strand of nucleic acid having a mismatch;

j) forming single-stranded DNA from said gene of said human sample and from a corresponding fragment of an allele specific for one of said mutations, electrophoresing said single-stranded DNAs on a non-denaturing polyacrylamide gel and comparing the mobility of said single-stranded DNAs on said gel to determine if said single-stranded DNA from said sample is shifted relative to said allele, wherein no shift in electrophoretic mobility of the single-stranded DNA relative to the allele indicates the presence of said mutation in said sample; and

k) forming a heteroduplex consisting of a first strand of nucleic acid selected from the group consisting of a genomic DNA fragment of said gene isolated from said sample, an RNA fragment isolated from said sample and a cDNA fragment made from mRNA from said sample and a second strand of a nucleic acid consisting of a corresponding gene allele fragment specific for one of said mutations and analyzing for the presence of a mismatch in said heteroduplex, wherein no mismatch indicates the presence of said mutation.

30. A method according to claim 29 wherein hybridization is performed *in situ*.

31. An isolated human polypeptide encoded by *SCN5A* comprising a mutation of SEQ ID NO:4 selected from the group consisting of D1114N, L1501V, delF1617, R1623L, E1784K and S1787N.

32. An antibody capable of binding the polypeptide of claim 31 but incapable of binding a wild-type polypeptide.

33. An antibody according to claim 32 wherein said antibody is a monoclonal antibody.

34. A method of assessing a risk in a human subject for long QT syndrome which comprises screening said subject for a mutation in *SCN5A* by comparing the sequence of said

SCN5A or its expression products isolated from a tissue sample of said subject with a wild-type sequence of said *SCN5A* or its expression products, wherein a mutation in the sequence of the subject indicates a risk for long QT syndrome.

35. The method of claim 34 wherein said expression product is selected from mRNA of said gene or a polypeptide encoded by said gene.

36. The method of claim 34 wherein one or more of the following procedures is carried out:
(a) observing shifts in electrophoretic mobility of single-stranded DNA from said sample on non-denaturing polyacrylamide gels;
(b) hybridizing a probe to genomic DNA isolated from said sample under conditions suitable for hybridization of said probe to said gene;
(c) determining hybridization of an allele-specific probe to genomic DNA from said sample;
(d) amplifying all or part of said gene from said sample to produce an amplified sequence and sequencing the amplified sequence;
(e) determining by nucleic acid amplification the presence of a specific mutant allele in said sample;
(f) molecularly cloning all or part of said gene from said sample to produce a cloned sequence and sequencing the cloned sequence;
(g) determining whether there is a mismatch between molecules (1) said gene genomic DNA or mRNA isolated from said sample, and (2) a nucleic acid probe complementary to the human wild-type gene DNA, when molecules (1) and (2) are hybridized to each other to form a duplex;
(h) amplification of said gene sequences in said sample and hybridization of the amplified sequences to nucleic acid probes which comprise wild-type gene sequences;
(i) amplification of said gene sequences in said tissue and hybridization of the amplified sequences to nucleic acid probes which comprise said mutant gene sequences;
(j) screening for a deletion mutation;
(k) screening for a point mutation;
(l) screening for an insertion mutation;

(m) determining *in situ* hybridization of said gene in said sample with one or more nucleic acid probes which comprise said gene sequence or a mutant sequence of said gene;

(n) immunoblotting;

(o) immunocytochemistry;

(p) assaying for binding interactions between said gene protein isolated from said tissue and a binding partner capable of specifically binding the polypeptide expression product of a mutant allele and/or a binding partner for the polypeptide; and

(q) assaying for the inhibition of biochemical activity of said binding partner.

37. A nucleic acid probe which hybridizes to the isolated DNA of claim 26 under conditions at which it will not hybridize to wild-type DNA.

38. A method for diagnosing a mutation which causes long QT syndrome comprising hybridizing a probe of claim 37 to a patient's sample of DNA or RNA, the presence of a hybridization signal being indicative of long QT syndrome.

39. A method according to claim 38 wherein the patient's DNA or RNA has been amplified and said amplified DNA or RNA is hybridized with a probe of claim 37.

40. A method according to claim 38 wherein said hybridization is performed *in situ*.

41. A method according to claim 38 wherein said assay is performed using nucleic acid microchip technology.

42. A method for diagnosing a mutation which causes long QT syndrome comprising amplifying a region of gene or RNA for *SCN5A* and sequencing the amplified gene or RNA wherein long QT syndrome is indicated by any one or more mutations selected from the group consisting of G3340A, C4501G, del4850-4852, G4868T, G5349A and G5360A.

43. A method for diagnosing a mutation which causes long QT syndrome comprising identifying a mismatch between a patient's DNA or RNA and a wild-type DNA or RNA probe wherein said probe hybridizes to a region of DNA or RNA wherein said region comprises a mutation of SEQ ID NO:3 selected from the group consisting of G3340A, C4501G, del4850-4852, G4868T, G5349A and G5360A.

44. The method of claim 43 wherein the mismatch is identified by an RNase assay.

45. A method for diagnosing long QT syndrome said method consisting of an assay for the presence of mutant SCN5A polypeptide in a patient by reacting a patient's sample with an antibody of claim 32, the presence of a positive reaction being indicative of long QT syndrome.

46. The method of claim 45 wherein said assay comprises immunoblotting.

47. The method of claim 45 wherein said assay comprises an immunocytochemical technique.

48. A method for diagnosing long QT syndrome, said method comprising analyzing a SCN5A polypeptide, a mutation in said polypeptide being indicative of long QT syndrome wherein said mutation is a mutation selected from the group consisting of D1114N, L1501V, delF1617, R1623L, E1784K and S1787N.

49. A method to screen for drugs which are useful in treating a person with a mutation in *SCN5A* wherein said mutation is selected from the group consisting of G3340A, C4501G, del4850-4852, G4868T, G5349A and G5360A, said method comprising:

a) placing a first set of cells expressing SCN5A with a mutation, wherein said mutation is selected from the group consisting of D1114N, L1501V, delF1617, R1623L, E1784K and S1787N, into a bathing solution;

b) inducing a first induced Na^+ current in the cells of step (a);

c) measuring said first induced Na^+ current;

d) placing a second set of cells expressing wild-type SCN5A into a bathing solution;

e) inducing a second induced Na^+ current in the cells of step (d);

f) measuring said second induced Na^+ current;

g) adding a drug to the bathing solution of step (a);

h) inducing a third induced Na^+ current in the cells in step (g);

i) measuring said third induced Na^+ current; and

j) determining whether the third induced Na^+ current is more similar to the second induced Na^+ current than is the first induced Na^+ current, wherein drugs resulting in a third induced Na^+ current which is closer to the second induced Na^+ current than is the first induced Na^+ current are useful in treating said persons.

50. An isolated DNA encoding an SCN5A polypeptide of SEQ ID NO:4 having a mutation selected from the group consisting of D1114N, L1501V, delF1617, R1623L, E1784K and S1787N.